UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/155,676	01/04/1999	DAVID WALLACH	WALLACH=21	8997

1444 7590 09/05/2002

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
EPPS, JANET L	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 09/05/2002

35

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/155,676	Applicant(s) WALLACH ET AL.	
	Examiner Janet Epps	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply,within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-16,20-22,30,43-60 and 62-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *52-54 and 65-68* is/are allowed.

6)☒ Claim(s) *13-16,20-22,30,43-51,55-60,62-64 and 69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 January 1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

3. Applicant's arguments set forth in the After-Final Amendments of 4-17-2002, 5-10-2002, and 7-18-02 with respect to the rejection of claims 13-16, 20-22, 30, 43-60, and 62-68 under 35 USC 112, 1st paragraph for lack of enablement, have been considered but are moot in view of the new ground(s) of rejection.

4. Claim 13-16, 20-22, 30, 43-50, and 55-60, 62-64, and 69 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims read on, for example, a polypeptide comprising (a) an amino acid fragment of either the polypeptide sequence of SEQ ID NO: 2, an amino acid sequence encoded by the nucleotide sequence of SEQ ID NO: 6, or the amino acid sequence of SEQ ID NO:5, which fragment binds to TRAF2 and either inhibits or increases the activity of NF-kB; (b) an analog of said fragment having no more than 10 changes in the amino acid sequence; and (c) a derivative of said fragment or analog of said fragment. Additionally, the instant invention reads on fragments of a DNA sequence according to SEQ ID NO: 1, 6, or 4, and DNA sequences

capable of hybridizing to said DNA sequence or fragments, wherein said DNA sequence encodes a polypeptide that binds to TRAF2 and either inhibits or increases the activity of NF-kB.

However, the specification as filed does not indicate what substitutions, deletions, or insertions of an amino acid are to be made to said fragments, or derivatives or analogs of said fragments wherein a polypeptide comprising said fragment is capable of binding TRAF2 and either inhibiting or increasing the activity of NF-kB. Moreover, the specification as filed does not sufficiently describe the DNA sequence fragments that are capable of encoding a polypeptide that binds to TRAF2 and either inhibits or increases the activity of NF-kB. Additionally, in regards to the DNA molecules that hybridize under moderately stringent conditions, such that said molecule encodes a ppolypeptide that are capable of encoding a polypeptide that binds to TRAF2 and either inhibits or increases the activity of NF-kB, Applicants have merely described the instant application by means of describing the method of isolating said sequences.

See the January 5, 2001 (Vol. 66, No. 4, pages 1099-1111) Federal Register for the Guidelines for Examination of Patent Applications Under the 35 USC 112 ¶ 1, "Written Description" Requirement. These guidelines state that: "To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical

formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that applicant was in possession of the claimed invention."

Although applicants provide an assay for isolating nucleic acids which encode polypeptides that bind Traf2 and either inhibits or increases the activity of NF-kB, without knowledge of the all the structures of the nucleic acid molecules one of skill in the art would have to resort to trial and error experimentation in order to determine the structures of all possible nucleic acids encoding polypeptides having the desired function. It is inappropriate to describe a chemical compound by means of describing its method of isolation, as stated above, possession is demonstrated by describing the claimed invention by means of drawings or by structural chemical formula.

Furthermore, the specification as filed provides no indication of what specific amino acid substitutions, deletions, insertions, or amino acid modifications must be made to the polypeptides of the instant invention in order to isolate those polypeptides with the claimed activity, specifically those which modulate NF-κB activity and bind TRAF2. It is apparent that further experimentation is necessary to isolate the compounds of the present invention, specifically to determine what amino acid substitutions, deletions, and/or insertions are necessary to isolate the polypeptides encompassed by the present invention.

Although, it is accepted that the amino acid sequence of a polypeptide determines its structural and functional properties, predicting a polypeptide's structure and function from mere sequence data remains an elusive task. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid

substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions, deletions, or insertions, can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of functional activity. These regions can tolerate only relatively conservative substitutions or no substitutions. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for polypeptides according to the present invention, this is not adequate guidance as to the nature of active fragments, derivatives, or analogs of said fragments or derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (see for example, Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2).

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein sequence. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a known sequence (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in under-predictions of functionality of a new protein and (2) over-predictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity.

Due to the limited structural information regarding what amino acid residues may be deleted, substituted or inserted into the polypeptides according to the present invention, wherein said polypeptide retains the ability to bind TRAF2 and inhibit or increase the activity of NF-kB, and the level of unpredictability associated with protein structure and predicting protein function and the lack of guidance thereof in the specification as filed, it is concluded that Applicant's disclosure is insufficient to adequately describe the genus of polypeptides encompassed by the claimed invention. With the exception of the amino acid sequences according to SEQ ID NO: 2, an amino acid sequence encoded by the nucleotide sequence of SEQ ID NO: 6, or the amino acid sequence of SEQ ID NO:5, Applicant's specification does not provide sufficient description for the broad genus of polypeptides encompassed by the instant claims since possession can not be

shown by providing a means to isolate a compound. What is required is an actual description of the claimed invention, particularly by means of drawings or structural chemical formulas that show that the invention was complete at the time of filing of the claimed invention.

Conclusion

5. Claims 52-54, and 65-68 are free of the prior art searched.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps whose telephone number is 703-308-8883. The examiner can normally be reached on Mondays through Friday, 9:00AM to 6:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703)-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L. Epps
Patent Examiner
August 27, 2002

SEAN McGARRY
PRIMARY EXAMINER
1635